

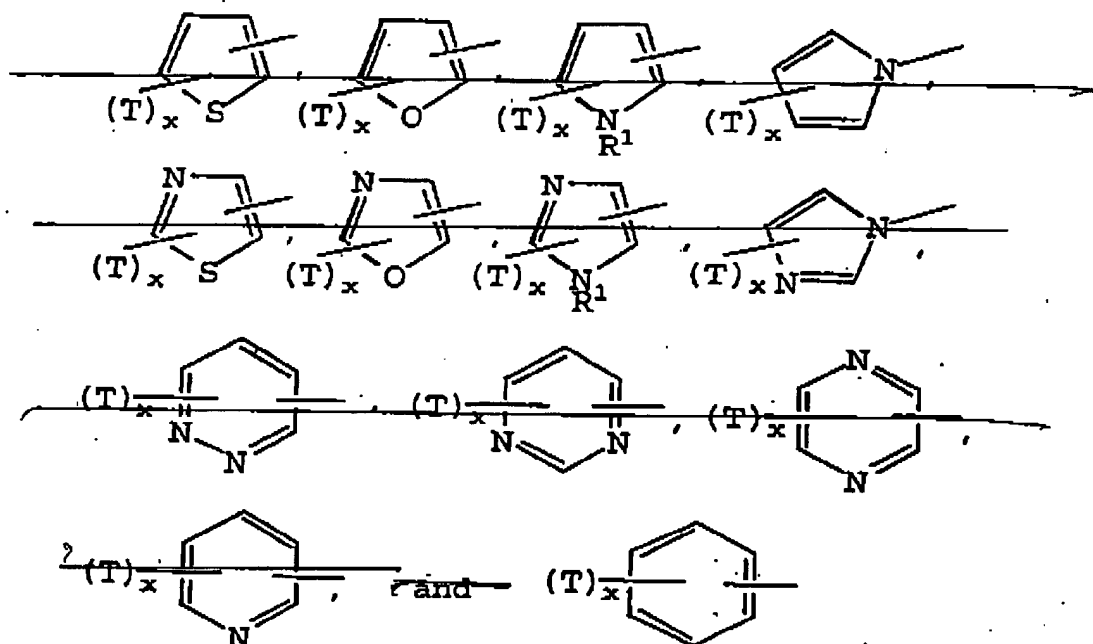
MARK UP OF AMENDED CLAIMS - USSN 09/719,320

1. (Amended) Method of using therapeutically effective amounts of compounds of the generalized formula (I):

(T)<sub>x</sub>A-B-D-E-CO<sub>2</sub>H wherein (T)<sub>x</sub>A ~~is a~~ represents a substituted or unsubstituted aromatic or heteroaromatic moiety selected from the group consisting of:

(a) ~~(T)<sub>x</sub>A represents a substituted or unsubstituted aromatic or heteroaromatic moiety selected from the group consisting of:~~

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wherein R<sup>1</sup> represents H or alkyl of 1 - 3 carbons; and

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each T represents a substituent group, independently selected from the group consisting of:

- \* the halogens -F, -Cl, -Br, and -I;
- \* alkyl of 1 - 10 carbons;
- \* hal alkyl f 1 - 10 carbons;

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- alkenyl of 2 - 10 carbons;
- alkynyl of 2 - 10 carbons;
- $-(CH_2)_pQ$ , wherein  
p is 0 or an integer 1 - 4,
- -alkenyl-Q, wherein  
said alkenyl moiety ~~comprises~~ consists of 2 - 4 carbons, and  
-alkynyl-Q, wherein  
said alkynyl moiety ~~comprises~~ consists of 2 - 7 carbons; and

Q is selected from the group consisting of aryl of 6 - 10 carbons, heteroaryl ~~comprising~~ consisting of 4 - 9 carbons and at least one N, O, or S heteroatom, -CN, -CHO, -NO<sub>2</sub>, -CO<sub>2</sub>R<sup>2</sup>, -OCOR<sup>2</sup>, -SOR<sup>3</sup>, -SO<sub>2</sub>R<sup>3</sup>, -CON(R<sup>4</sup>)<sub>2</sub>, -SO<sub>2</sub>N(R<sup>4</sup>)<sub>2</sub>, -C(O)R<sup>2</sup>, -N(R<sup>4</sup>)<sub>2</sub>, -N(R<sup>2</sup>)COR<sup>2</sup>, -N(R<sup>2</sup>)CO<sub>2</sub>R<sup>3</sup>, -N(R<sup>2</sup>)CON(R<sup>4</sup>)<sub>2</sub>, -CHN<sub>4</sub>, -OR<sup>4</sup>, and -SR<sup>4</sup>;

wherein

R<sup>2</sup> represents H;

alkyl of 1 - 6 carbons;  
aryl of 6 - 10 carbons;  
heteroaryl ~~comprising~~ consisting of 4 - 9 carbons and at least one N, O, or S heteroatom; or  
arylalkyl in which the aryl portion contains 6-10 carbons and the alkyl portion ~~contains~~ consists of 1 - 4 carbons; or  
heteroaryl-alkyl in which the heteroaryl portion ~~comprises~~ consists of 4-9 carbons and at least one N, O, or S heteroatom and the alkyl portion ~~contains~~ consists of 1 - 4 carbons;

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R<sup>3</sup> represents alkyl of 1-4 carbons;  
aryl of 6-10 carbons;

heteroaryl ~~emprising~~ consisting of 4 - 9 carbons and at least one N, O, or  
S heteroatom; or  
arylalkyl in which the aryl portion ~~contains~~ consists of 6 - 10 carbons and  
the alkyl portion ~~contains~~ consists of 1 - 4 carbons; or  
heteroaryl-alkyl in which the heteroaryl portion ~~emprises~~ consists of 4 -  
9 carbons and at least one N, O, or S heteroatom and the alkyl  
portion ~~contains~~ consists of 1 - 4 carbons;

R<sup>4</sup> represents H;

alkyl of 1 - 12 carbons;  
aryl of 6 - 10 carbons;  
heteroaryl ~~emprising~~ consisting of 4 - 9 carbons and at least one N, O, or  
S heteroatom;  
arylalkyl in which the aryl portion ~~contains~~ consists of 6 - 10 carbons and  
the alkyl portion ~~contains~~ consists of 1 - 4 carbons;  
heteroaryl-alkyl in which the heteroaryl portion ~~emprises~~ consists of 4 -  
9 carbons and at least one N, O, or S heteroatom and the alkyl  
portion ~~contains~~ consists of 1-4 carbons;

alkenyl of 2 - 12 carbons;

alkynyl of 2 - 12 carbons;

-(CqH<sub>2</sub>qO)<sub>r</sub>R<sup>5</sup> wherein q is 1-3; r is 1 - 3; and R<sup>5</sup> is H

provided q is greater than 1, or alkyl of 1 - 4 carbons, or  
phenyl;

alkylenethio terminated with H, alkyl of 1-4 carbons, or phenyl;

alkyleneamino terminated with H, alkyl of 1-4 carbons, or phenyl;

-(CH<sub>2</sub>)<sub>s</sub>X wherein s is 1 - 3 and X is halogen;

-C(O)OR<sup>2</sup>; or

-C(O)R<sup>2</sup>;

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and with the provisos that a) when two  $R^4$  groups are situated on a nitrogen, they may be joined by a bond to form a heterocycle, and

b) unsaturation in a moiety which is attached to Q or which is part of Q is separated from any N, O, or S of Q by at least one carbon atom, and

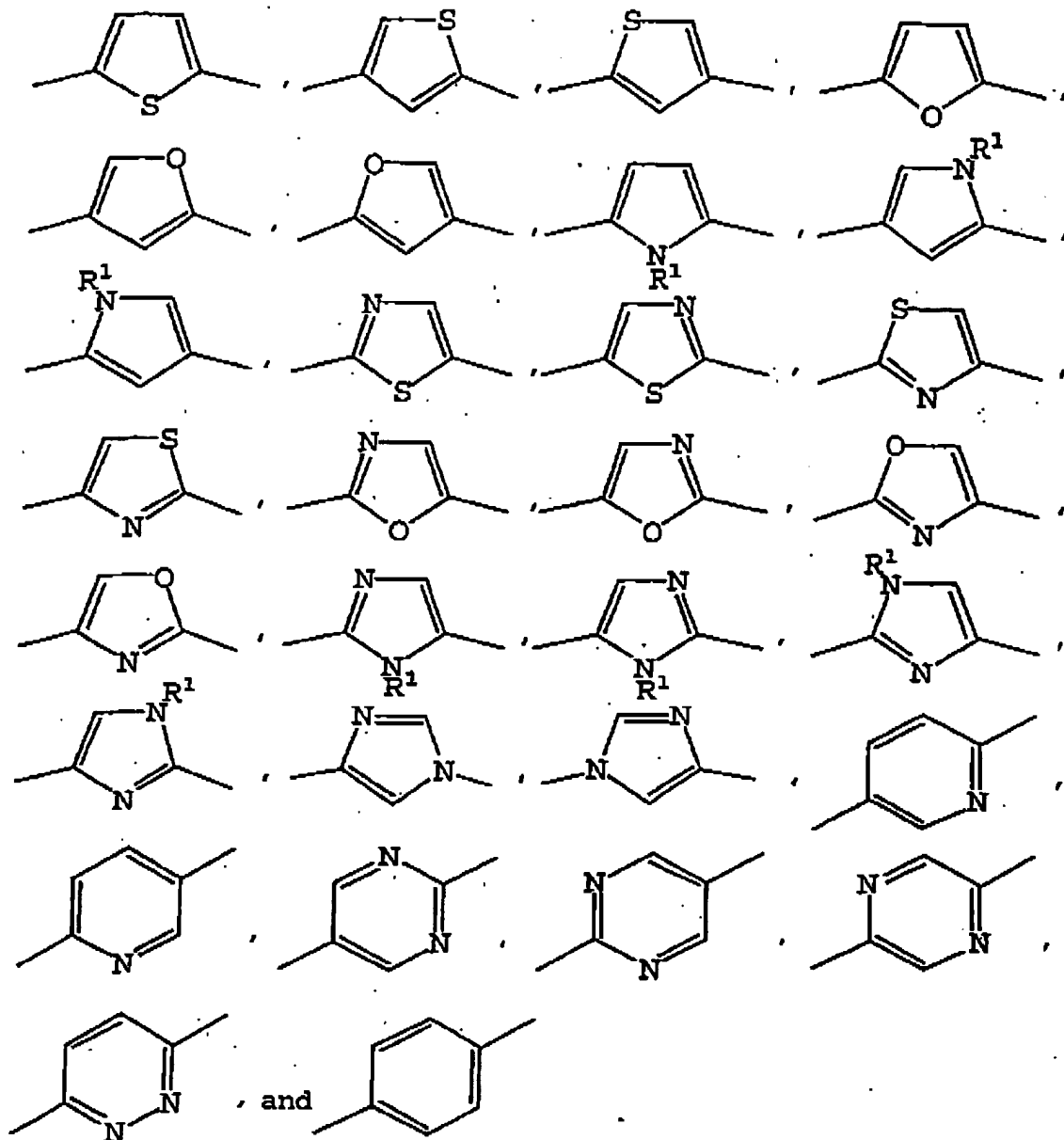
x is 0,1,or2;

(b) B represents a bond or an optionally substituted aromatic or hetero-aromatic ring ~~containing~~ consisting of either 0, 1 or 2 ~~0-2~~ substituents T groups, which ~~substituents T groups~~ substituents T groups may independently have the meaning specified under (a), the B rings being selected from the group consisting of:

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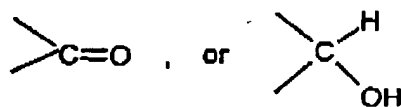
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wherein  $R^1$  is as defined above and each  $R^1$  may be the same or different:

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(c) D represents



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- (d) E represents a chain of  $n$  carbon atoms bearing  $m$  substituents  $R^6$  groups, wherein said  $R^6$  groups are independent substituents, or constitute spiro or nonspiro rings in which a) two groups  $R^6$  are joined, and taken together with the chain atom(s) to which said two  $R^6$  group(s) are attached, and any intervening chain atoms, constitute a 3 - 7 membered ring, or b) one group  $R^6$  is joined to the chain on which said one group  $R^6$  resides, and taken together with the chain atom(s) to which said  $R^6$  group is attached, and any intervening chain atoms, constitutes

a 3 - 7 membered ring; and wherein

$n$  is 2 or 3;

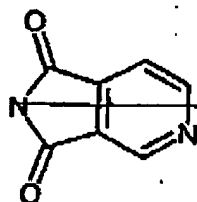
$m$  is an integer of 1 - 3;

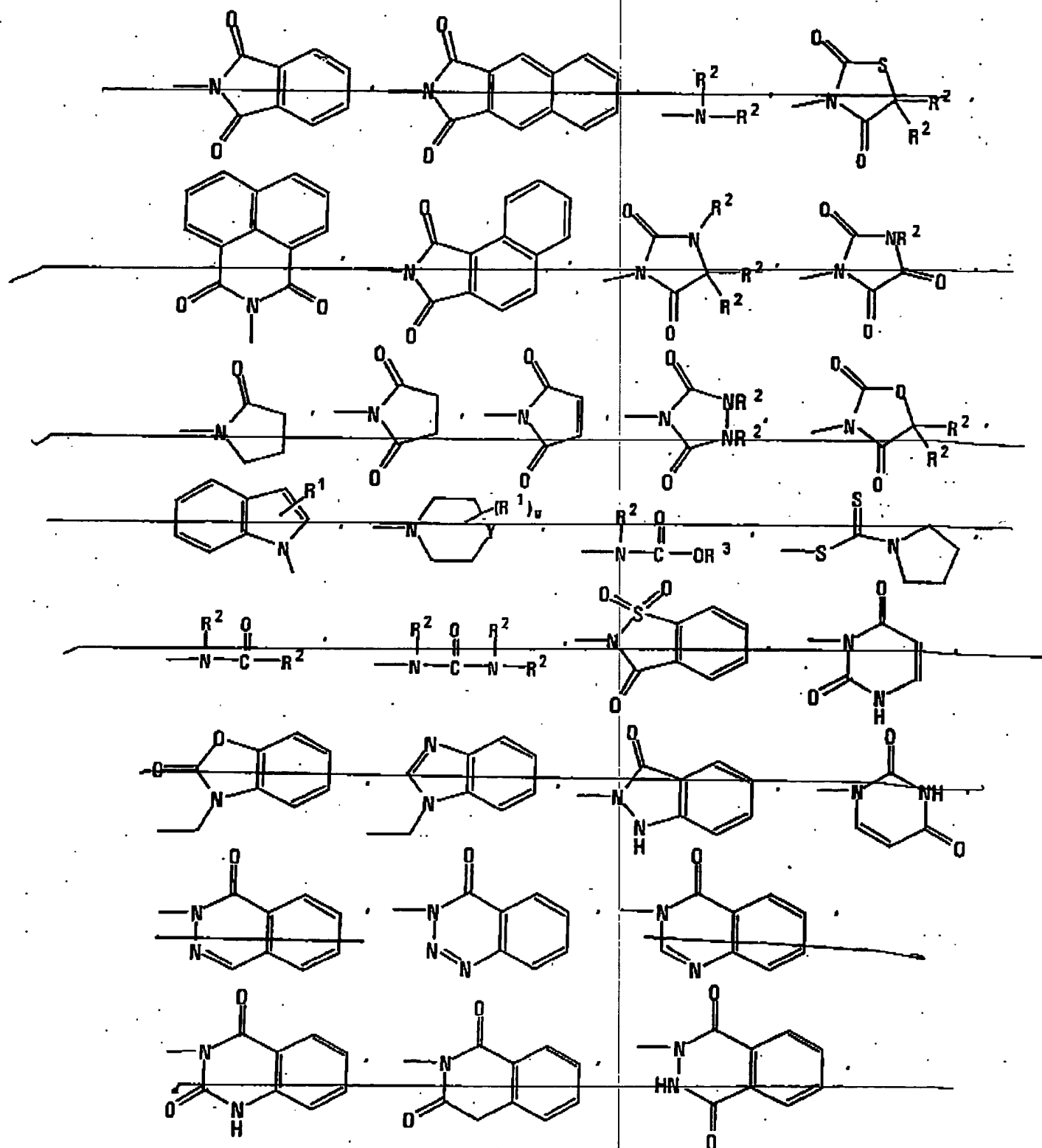
each group  $R^6$  is independently selected from the group consisting of:

- fluorine;
- hydroxyl, with the proviso that a single carbon may bear no more than one hydroxyl substituent
- alkyl of 1 - 10 carbons;
- aryl of 6 - 10 carbons;
- heteroaryl comprising 4 - 9 carbons and at least one N, O, or S heteroatom;
- arylalkyl wherein the aryl portion contains 6 - 10 carbons and the alkyl portion contains 1 - 8 carbons;

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- heteroaryl-alkyl wherein the heteroaryl portion ~~comprises~~ consists of 4 - 9 carbons and at least one N, O, or S heteroatom, and the alkyl portion ~~contains~~ consists of 1 - 8 carbons;
- alkenyl of 2 - 10 carbons;
- aryl-alkenyl wherein the aryl portion ~~contains~~ consists of 6 - 10 carbons and the alkenyl portion ~~contains~~ consists of 2 - 5 carbons;
- heteroaryl-alkenyl wherein the heteroaryl portion ~~comprises~~ consists of 4 - 9 carbons and at least one N, O, or S heteroatom and the alkenyl portion ~~contains~~ consists of 2 - 5 carbons;
- alkynyl of 2 - 10 carbons;
- aryl-alkynyl wherein the aryl portion contains 6 - 10 carbons and the alkynyl portion ~~contains~~ consists of 2 - 5 carbons;
- heteroaryl-alkynyl wherein the heteroaryl portion ~~comprises~~ consists of 4 - 9 carbons and at least one N, O, or S heteroatom and the alkynyl portion contains 2 - 5 carbons;
- $-(CH_2)_tR^7$  wherein  
t is 0 or an integer of 1 - 5; and  
R<sup>7</sup> is selected from the group consisting of







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and corresponding heteroaryl moieties in which the aryl portion of an arylcontaining  $R^7$  group comprises 4 - 9 carbons and at least one N, O or S heteroatom;

wherein

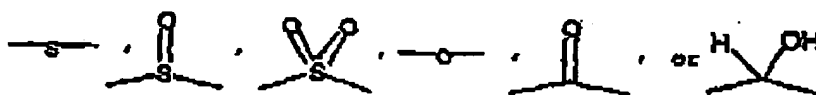
Y represents O or S;

$R^1$ ,  $R^2$ , and  $R^3$  are as defined above and each  $R^1$ ,  $R^2$  or  $R^3$  may be the same or different; and

•  $-(CH_2)_vZR^8$  wherein

v is 0 or an integer of 1 to 4;

and Z represents



$R^8$  is selected from the group consisting of: alkyl

of 1 to 12 carbons;

aryl of 6 to 10 carbons;

heteroaryl ~~comprising~~ consisting of 4 - 9 carbons and at least one N, O, or S heteroatom;

arylalkyl wherein the aryl portion ~~contains~~ consists of 6 to 10 carbons and the alkyl portion ~~contains~~ consists of 1 to 4 carbons;

heteroaryl-alkyl wherein the aryl portion ~~comprises~~ consists of 4 - 9 carbons

and at least one N, O, or S heteroatom and the alkyl portion ~~contains~~ consists of 1 - 4 carbons;

$-C(O)R^9$  wherein  $R^9$  represents alkyl of 2 - 6 carbons, aryl of 6 - 10 carbons, heteroaryl of comprising 4 - 9 carbons and at least one N, O, or S heteroatom, or arylalkyl in which the aryl portion ~~contains~~ consists of 6 - 10 carbons or is heteroaryl ~~comprising~~ consisting of 4 - 9

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carbons and at least one N, O, or S heteroatom, and the alkyl portion ~~contains~~ consists of 1-4 carbons;

and with the provisos that

- when  $R^8$  is  $-C(O)R^9$ , Z is S or O;
- when Z is O,  $R^8$  may also be  $-(C_qH_{2q}O)_rR^5$  wherein q, r, and  $R^5$  are as defined above; and

- $-(CH_2)_wSiR^3$  wherein  
w is an integer of 1 to 3; and  
 $R^{10}$  represents alkyl of 1 to 2 carbons;

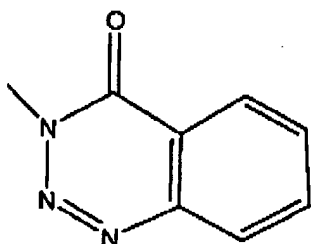
and with the proviso that

- aryl or heteroaryl portions of any of said T or  $R^6$  groups optionally may bear up to two substituents selected from the group consisting of  
 $-(CH_2)_yC(R^4)(R^3)OH$ ,  $-(CH_2)_yOR^4$ ,  $-(CH_2)_ySR^4$ ,  $-(CH_2)_yS(O)_2R^4$ ,  
 $-(CH_2)_yS(O)_2R^4$ ,  $-(CH_2)_ySO_2N(R^4)_2$ ,  $-(CH_2)_yN(R^4)_2$ ,  
 $-(CH_2)_yN(R^4)COR^3$ ,  $-OC(R^4)_2O-$  in which both oxygen atoms are connected to the aryl ring,  $-(CH_2)_yCOR^4$ ,  $-(CH_2)_yCON(R^4)_2$ ,  
 $-(CH_2)_yCO_2R^4$ ,  $-(CH_2)_yOCOR^4$ , -halogen, -CHO,  $-CF_3$ ,  $-NO_2$ , -CN, and  
 $-R^3$ , wherein  
y is 0-4; and  
 $R^3$  and  $R^4$  are defined as above, and each  $R^3$  or  $R^4$  may be the same or different; and any two  $R^4$  which are attached to one nitrogen may be joined to form a heterocycle;
- and wherein at least one pharmaceutically acceptable salt ~~salts and prodrugs thereof is administered~~ for the treatment and prevention of cerebral diseases.

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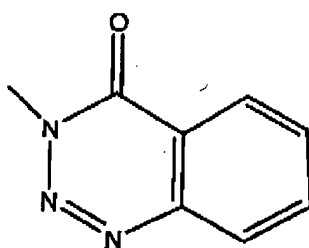
2. Method ~~of using compounds of the generalized formula (1)~~ according to claim 1,

wherein  $R^6$  is  $-(CH_2)_tR^7$ , in which  $t$  is 0 or an integer 1-5, and  $R^7$  is a group of the formula



and wherein at least one pharmaceutically acceptable salt ~~salts and prodrugs~~  
~~thereof is administered~~ for the treatment and prevention of cerebral diseases.

3. Method ~~of using compounds of the generalized formula (1)~~ according to claim 1, where E represents a chain of 2 carbon atoms bearing 1 substituent  $R^6$ , and wherein  $R^6$  is  $-(CH_2)_tR^7$ , in which  $t=0$  or an integer 1-5, and  $R^7$  is a group of the formula

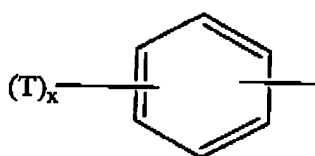


and wherein at least one pharmaceutically acceptable salt ~~salts and prodrugs~~  
~~thereof is administered~~ for the treatment and prevention of cerebral diseases.

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4. Method of using compounds of the generalized formula (1) according to claim 1, wherein

(a)  $(T)_x A$  represents a group of the formula



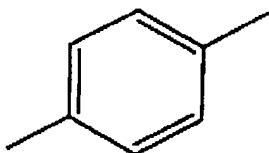
wherein

T represents a substituent group independently selected from the group consisting of

- the halogens -F, -Cl, -Br, and -I;
- alkyl of 1 - 10 carbons; and
- $-(CH_2)_p Q$ , wherein p is 0 or an integer 1 - 4, and Q is  $-OR^4$ , wherein  $R^4$  represents alkyl of 1-12 carbons;

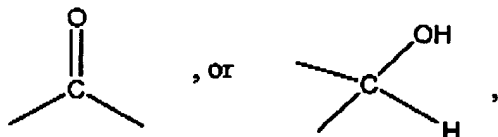
and x = 0, 1 or 2;

(b) B represents a group of the formula



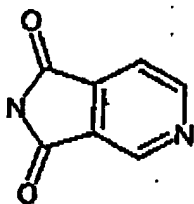
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(c) D represents



(d) (e) E represents a group of the formula  $-\text{CH}_2-\text{CHR}^6-$ , wherein

$\text{R}^6$  is a group of the formula  $-(\text{CH}_2)_t\text{R}^7$ ,  
 wherein t is 0 or an integer of 1 - 5; and  
 $\text{R}^7$  is a group of the formula



with the proviso that the aryl portion of said  $\text{R}^6$  group optionally may bear up to two substituents selected from the group consisting of -halogen, -CHO, -CF<sub>3</sub>, -NO<sub>2</sub>, and -CN,

and wherein at least one pharmaceutically acceptable salt ~~salts and prodrugs~~  
 thereof is administered for the treatment and prevention of cerebral diseases.